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US60/532,130 2003-12-23 <150>

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Ser Met Val Trp Ser Ile Asn Leu Thr Ala Gly Met Tyr Cys Ala Ala

Leu Glu Ser Leu Ile Asn Val Ser Gly Cys Ser Ala Ile Glu Lys Thr

Gln Arg Met Leu Ser Gly Phe Cys Pro His Lys Val Ser Ala Gly Gln 65 70 75 80

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Leu Glu Ser Leu Ile Asn Val Ser Gly Cys Ser Ala Ile Glu Lys Thr 50 60

Gln Arg Met Leu Ser Gly Phe Cys Pro His Lys Val Ser Ala Gly Gln 65 70 75 80

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Gln Arg Ala Thr Ile Ser Cys Arg Ala Ser Lys Ser Val Asp Ser Tyr 20 25 30

Gly Asn Ser Phe Met His Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro 35 40 45

Lys Leu Leu Ile Tyr Leu Ala Ser Asn Leu Glu Ser Gly Val Pro Ala 50 60

Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr Leu Thr Ile Asp 65 70 75

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Ser Val Asn Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Leu 35 40 45

Gly Met Ile Trp Gly Asp Gly Lys Ile Val Tyr Asn Ser Ala Leu Lys 50 60

Ser Arg Leu Asn Ile Ser Lys Asp Ser Ser Lys Ser Gln Val Phe Leu 65 70 75 80

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Gly Met Ile Trp Gly Asp Gly Ser Thr Ala Tyr Asn Ser Ala Leu Lys 50 60

Ser Arg Leu Ser Ile Ser Lys Asp Asn Ser Lys Ser Gln Ile Phe Leu 70 75 80

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Gly Met Ile Trp Gly Asp Gly Ser Thr Ala Tyr Asn Ser Ala Leu Lys 50 55 60

Ser Arg Leu Ser Ile Ser Lys Asp Asn Ser Lys Ser Gln Ile Phe Leu

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Trp	Ile	Asn 35	Trp	Ile	Lys	Gln	Arg 40	Pro	Glу	Gln	Gly	Leu 45	Glu	Trp	Ile	
Glу	His 50	Ile	Аlа	Pro	Gly	Ser 55	Gly	Ser	Thr	туr	Phe 60	Asn	Glu	Met	Phe	
Lys 65	Gly	Lys	Аla	Thr	Leu 70	Thr	Val	Asp	Thr	Ser 75	Ser	ser	Thr	Ala	туг 80	
Ile	Gln	Leu	Ser	Ser 85	Leu	Ser	Ser	Glu	Asp 90	Ser	Ala	۷a٦	Tyr	Phe 95	Cys	
Аlа	Arg	Ser	Asp 100		Phe	Leu	Ser	Tyr 105	Ala	Met	Asp	Tyr	Trp 110	Glу	Gln	
Gly	Thr	Ser 115		Thr	۷al	ser	Ser 120									
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cagaaco	caga aggccccgct ctgcaatggc agcatggtgt ggagcatcaa cctgacagct	180
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Gly Gln Ser Phe Met His Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro 35 40 45

Lys Leu Leu Ile Tyr Leu Ala Ser Asn Leu Glu Ser Gly Val Pro Asp 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser 65 70 75 80

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Thr Leu Thr Leu Thr Cys Thr Gly Ser Gly Phe Ser Leu Ser Ala Tyr 20 25 30

Ser Val Asn Trp Ile Arg Gln Pro Pro Gly Lys Ala Leu Glu Trp Leu 35 40 45

Ala Met Ile Trp Gly Asp Gly Lys Ile Val Tyr Asn Ser Ala Leu Lys $50 \hspace{1.5cm} 55 \hspace{1.5cm} 60$

Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val Leu 65 70 75 80

Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr Cys Ala 85 90 95

Val Asp Gly Tyr Tyr Pro Tyr Ala Met Lys Asn Trp Gly Gln Gly Ser 100 105

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Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Lys Ser Val Asp Ser Tyr 20 25 30

Gly Gln Ser Phe Met His Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro 35 40 45

Lys Leu Leu Ile Tyr Leu Ala Ser Asn Leu Glu Ser Gly Val Pro Asp 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser 65 70 75 80

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Ala Met Ile Trp Gly Asp Gly Lys Ile Val Tyr Asn Ser Ala Leu Lys 50 60

Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val Val Leu 65 70 75 80

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Gly Gln Ser Phe Met His Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Leu Ala Ser Asn Leu Glu Ser Gly Val Pro Asp 50 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser 65 70 75 80

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Ala Met Ile Trp Gly Asp Gly Lys Ile Val Tyr Asn Ser Ala Leu Lys 50 60

Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val Val Leu 70 75 80 Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr Cys Ala 85 90 95 Val Asp Gly Tyr Tyr Pro Tyr Ala Met Lys Asn Trp Gly Gln Gly Ser 100 105 110 Leu Val Thr Val Ser Ser 115 <210> 99 15 <211> <212> PRT ARTIFICIAL <220> <223> CDR-L1 228B/C <400> 99 Arg Ala Ser Lys Ser Val Asp Ser Tyr Gly Asn Ser Phe Met His 1 10 15<210> 100 <211> 15 <212> PRT <213> ARTIFICIAL <220> <223> CDR-L1 VARIANT 1 <400> 100 Arg Ala Ser Lys Ser Val Asp Ser Tyr Gly Gln Ser Phe Met His 1 10 15<210> 101 <211> <212> 15 PRT <213> ARTIFICIAL <220> CDR-L1 VARIANT 2 <223> <400> 101 Arg Ala Ser Lys Ser Val Asp Ser Tyr Gly Gln Ser Phe Leu His 1 10 15<210> <211> 102 15 PRT ARTIFICIAL <220> CDR-L1 VARIANT 3 <223>

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Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Lys Ser Val Asp Ser Tyr 20 25 30

Gly Asn Ser Phe Met His Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro 35 40 45

Lys Leu Leu Ile Tyr Leu Ala Ser Asn Leu Glu Ser Gly Val Pro Asp $50 \hspace{1.5cm} 55 \hspace{1.5cm} 60$

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser 65 70 75 80

Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Asn Asn 85 90 95

Glu Asp Pro Arg Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg 100 105 110

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Thr Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser Ala Tyr 20 25 30

Ser Val Asn Trp Ile Arg Gln Pro Pro Gly Lys Ala Leu Glu Trp Leu 35 40 45

Ala Met Ile Trp Gly Asp Gly Lys Ile Val Tyr Asn Ser Ala Leu Lys 50 60

Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val Val Leu 65 70 75 80

Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr Cys Ala 85 90 95

Gly Asp Gly Tyr Tyr Pro Tyr Ala Met Asp Asn Trp Gly Gln Gly Ser 100 105 110

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Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Lys Ser Val Asp Ser Tyr 20 25 30

Gly Asn Ser Phe Met His Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro 35 40 45

Lys Leu Leu Ile Tyr Leu Ala Ser Asn Leu Glu Ser Gly Val Pro Asp 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser 65 70 75 80

Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Asn Asn 85 90 95

Glu Asp Pro Arg Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg 100 105 110

<210> 145

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Thr Leu Thr Leu Thr Cys Thr Gly Ser Gly Phe Ser Leu Ser Ala Tyr 20 25 30

Ser Val Asn Trp Ile Arg Gln Pro Pro Gly Lys Ala Leu Glu Trp Leu 35 40 45

Ala Met Ile Trp Gly Asp Gly Lys Ile Val Tyr Asn Ser Ala Leu Lys 50 60

Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val Val Leu 70 75 80

Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr Cys Ala 85 90 95

Val Asp Gly Tyr Tyr Pro Tyr Ala Met Asp Asn Trp Gly Gln Gly Ser 100 105 110

Leu Val Thr Val Ser Ser 115

146

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ARTIFICIAL

<220> <223>

VARIABLE HEAVY CHAIN RL-19

<400> 146

Gln Val Thr Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro Thr Gln
5 10 15

Thr Leu Thr Cys Thr Ser Ser Gly Phe Ser Leu Ser Ala Tyr 20 25 30

Ser Val Asn Trp Ile Arg Gln Pro Pro Gly Lys Ala Leu Glu Trp Leu 35 40 45

Ala Met Ile Trp Gly Asp Gly Lys Ile Val Tyr Asn Ser Ala Leu Lys 50 60

Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val Leu 65 70 75 80

Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr Cys Ala 85 90 95

Leu Asp Gly Tyr Tyr Pro Tyr Ala Met Asp Asn Trp Gly Gln Gly Ser 100 105

Leu Val Thr Val Ser Ser 115

<210> 147

<211> 118

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Gln Val Thr Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro Thr Gln
5 10 15

Thr Leu Thr Leu Thr Cys Thr Thr Ser Gly Phe Ser Leu Ser Ala Tyr 20 25 30

Ser Val Asn Trp Ile Arg Gln Pro Pro Gly Lys Ala Leu Glu Trp Leu 35 40 45

Ala Met Ile Trp Gly Asp Gly Lys Ile Val Tyr Asn Ser Ala Leu Lys 50 55 60

Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val Leu 70 75 80

Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr Cys Ala 85 90 95

Val Asp Gly Tyr Tyr Pro Tyr Ala Met Asp Asn Trp Gly Gln Gly Ser 100 105 110

Leu Val Thr Val Ser Ser 115

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<223> VARIABLE HEAVY CHAIN RL-8

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Gln Val Thr Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro Thr Gln
5 10 15

Thr Leu Thr Cys Thr Leu Ser Gly Phe Ser Leu Ser Ala Tyr 20 25 30

Ser Val Asn Trp Ile Arg Gln Pro Pro Gly Lys Ala Leu Glu Trp Leu 35 40 45

Ala Met Ile Trp Gly Asp Gly Lys Ile Val Tyr Asn Ser Ala Leu Lys 50 55 60

Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val Leu 70 75 80

Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr Cys Ala 85 90 95

Ser Asp Gly Tyr Tyr Pro Tyr Ala Met Asp Asn Trp Gly Gln Gly Ser 100 105 110

Leu Val Thr Val Ser Ser 115

<210> 149

<211> 118 <212> PRT

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<223> VARIABLE HEAVY CHAIN RL-45

<400> 149

Gln Val Thr Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro Thr Gln 1 10 15

Thr Leu Thr Leu Thr Cys Thr Thr Ser Gly Phe Ser Leu Ser Ala Tyr 20 25 30

Ser Val Asn Trp Ile Arg Gln Pro Pro Gly Lys Ala Leu Glu Trp Leu 35 40 45

Ala Met Ile Trp Gly Asp Gly Lys Ile Val Tyr Asn Ser Ala Leu Lys 50 60

Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val Leu 65 70 75 80

Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr Cys Ala 85 90 95

Thr Asp Gly Tyr Tyr Pro Tyr Ala Met Asp Asn Trp Gly Gln Gly Ser 100 105 110

Leu Val Thr Val Ser Ser

<210> 150

<211> 112 <212> PRT

<213> ARTIFICIAL

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<223> VARIABLE LIGHT CHAIN RL-36-L1,59

∠400<u>\</u> 150

Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ser Val Ser Leu Gly 10 15

Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Lys Ser Val Asp Ser Tyr 20 25 30

Gly Gln Ser Phe Met His Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro 35 40 45

Lys Leu Leu Ile Tyr Leu Ala Ser Asn Leu Glu Ser Gly Val Pro Asp 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser 65 70 75 80

Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Asn Asn 85 90 95

Glu Asp Pro Arg Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg 100 105 110

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<211> <212> PRT

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<400>

Gln Val Thr Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro Thr Gln
5 10 15

Thr Leu Thr Leu Thr Cys Thr Gly Ser Gly Phe Ser Leu Ser Ala Tyr 20 25 30

Ser Val Asn Trp Ile Arg Gln Pro Pro Gly Lys Ala Leu Glu Trp Leu 35 40 45

Ala Met Ile Trp Gly Asp Gly Lys Ile Val Tyr Asn Ser Ala Leu Lys 50 60

Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val Leu 65 70 75 80

Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr Cys Ala 85 90 95

Val Asp Gly Tyr Tyr Pro Tyr Ala Met Asp Asn Trp Gly Gln Gly Ser 100 105 110

Leu Val Thr Val Ser Ser 115

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<211> 248 <212> PRT

<213> ARTIFICIAL

<220> <223> SINGLE CHAIN FV

<400> 152

Gln Val Thr Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro Thr Gln
5 10 15 Thr Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser Ala Tyr 20 25 30 Ser Val Asn Trp Ile Arg Gln Pro Pro Gly Lys Ala Leu Glu Trp Leu 35 40 45 Ala Met Ile Trp Gly Asp Gly Lys Ile Val Tyr Asn Ser Ala Leu Lys 50 60 Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val Val Leu 65 70 75 80 Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr Cys Ala 85 90 95 Gly Asp Gly Tyr Tyr Pro Tyr Ala Met Asp Asn Trp Gly Gln Gly Ser 100 105 110 Leu Val Thr Val Ser Ser Gly Gly Ser Ser Arg Ser Ser Ser Gly 115 120 Gly Gly Gly Ser Gly Gly Gly Asp Ile Val Met Thr Gln Ser Pro 130 140 Asp Ser Leu Ser Val Ser Leu Gly Glu Arg Ala Thr Ile Asn Cys Arg 145 150 155 160 Ala Ser Lys Ser Val Asp Ser Tyr Gly Asn Ser Phe Met His Trp Tyr 165 170 175 Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Leu Ala Ser 180 185 Asn Leu Glu Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly 195 200 205 Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Val Ala 210 220 Val Tyr Tyr Cys Gln Gln Asn Asn Glu Asp Pro Arg Thr Phe Gly Gly 225 230 235 240 Gly Thr Lys Val Glu Ile Lys Arg 245